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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,523	10/24/2003	Nicholas G. Bacopoulos	24852-501 CIP4	9840

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EXAMINER	
DELACROIX MUIRHE, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/692,523	BACOPOULOS ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-28,30-36,38-43,45-50,52-57,59-63 and 95-157* is/are pending in the application.

4a) Of the above claim(s) *143-156* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 12-28, 30-36, 38-43, 45-50, 52-57, 59-63, 95-142* is/are rejected.

7)☒ Claim(s) *157* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. Claims 1-10, 12-28, 30-36, 38-43, 45-50, 52-57, 59-63, 95-142 are rejected under 35 U.S.C. 103(a) as being unpatentable over DiMartino, 6,905,669.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New claims 95-142 are rejected under 35 USC 103(a) for reasons given previously in the office action mailed Sep. 23, 2005. However, additional comments concerning these claims are made below.

Response to Amendment(s)

The following is responsive to applicant's amendment received Jan. 23, 2006.

Claims 11, 29, 37, 44, 51, 58, 64-94 are cancelled. New claims 95-157 are added.

Claims 1-10, 12-28, 30-36, 38-43, 45-50, 52-57, 59-63, 95-157 are currently pending.

Newly submitted claims 143-157 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: Claim 143 is directed to a method of treating myelodysplastic syndrome (MDS) in a subject by administering, orally an effective amount of SAHA. The method in claims 143-157 has a separate and distinct outcome from the expected outcome of any one or more of the other originally presented methods. For example, the expected result of a method of treating MDS is distinctly different from a method of treating chronic myeloid leukemia. Additionally, the method in claims 143-157 would be practiced in a distinctly different population of patients. While there may be incidental overlap in the groups of patients experiencing MDS and those experiencing, for example, leukemia, the therapeutic objective, endpoints and steps required to treat such dissimilar conditions are vastly

different and do not reasonably suggest the treatment of the other. Finally, the search for the method of claims 143-157 would not be required for the other originally presented claimed methods.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 143-157 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim 157 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim 157 has not been further treated on the merits.

The previous rejection of claims 66-68 under 35 USC 103(a) set forth in paragraph 2 of the office action mailed Sep. 23, 2005, is withdrawn in view of applicant's amendment and the remarks contained therein.

However, applicant's arguments traversing the rejection of claims ???? under 35 USC 103(a) over DiMartino set forth in paragraph 1 of the office action mailed Sep. 23, 2005 have been considered but are not found to be persuasive.

Said rejection is maintained essentially for the reasons given previously in the office action mailed Sep. 23, 2005 with the following additional comment.

Applicant argues that, in contrast to the pending claims, DiMartino fails to report any specific dosages or dosage schedules for oral administration of SAHA. Instead, DiMartino reports dosages only for intravenous administration and for HDAC inhibitors other than SAHA such as depsipeptide, phenylbutyrate and arginine butyrate. The examiner has provided no

indication of how artisans could use DiMartino's intravenous dosages for structurally unrelated drugs to derive the specifically claimed oral dosages and schedules for SAHA. DiMartino fails to teach or suggest the claimed elements, and no suggestion or motivation has been provided to modify DiMartino to obtain the instant claims.

Moreover, the claims methods of oral administration produce unexpected half-life for SAHA given the available knowledge in the art. Applicants show that oral administration of SAHA results in significantly longer half-life for the drug as compared to intravenous administration. The examiner is referred to page 79, lines 9-11; Tables 2 and 3 and Figure 10 of the instant application. Oral SAHA produces a two-to-three fold increase in half-life as compared to intravenous delivery. The increased half-life for oral SAHA produces sustained histone acetylation in patients. The half-life for oral SAHA is surprising in view of prior cancer drugs, many of which exhibit short half-life from oral dosage. Thus, even if DiMartino could be modified and applied against the current claims, the claimed methods of oral administration show unexpected advantages which could not have been known from the cite publication.

Said arguments have been considered but are not found to be persuasive.

Concerning applicant's arguments of unexpected results, the examiner respectfully submits that the data in the specification and Figure 10 do not clearly establish, on the record, evidence of unexpected results. When comparing Table 2 and Table 3, it is not clear how the data demonstrates unexpected results. While the data for the half-life of SAHA is clear, that is to the say the numbers for oral administration are much higher than intravenous administration, the data given for C_{max} and AUC are less convincing. On page 79, lines 9-11, applicant states that "the AUC ***taken together*** with the half-life shows that the overall bioavailability of oral SAHA is

better than that of IV SAHA." However, the specification fails to further elaborate on what is meant by "taken together." Moreover, applicant has not shown the calculations done to arrive at the data shown in the Tables. Applicants are invited to make a showing of the calculations, which were made to arrive at the data in the Tables and how the data demonstrates unexpected results of oral administration compared to intravenous administration of SAHA.

Additionally, the examiner respectfully notes that applicants are comparing oral administration of 200 mg in a single capsule versus 200 mg of SAHA administered as an IV infusion. In the case of the oral administration, the 200 mg is administered all at once, whereas administration via infusion occurs over a period of time and the 200 mg is not made available to the subject all at once. Could the data obtained in the specification result from the difference in availability of the 200 mg of SAHA? Would a more accurate comparison involve a bolus injection of SAHA rather an infusion injection? Absent further evidence and clarification to the contrary, the examiner respectfully submits that the data provided in the specification does not demonstrate evidence of unexpected results.

Please note, according to MPEP 716.02(b), "[t]he evidence relied *>upon< should establish 'that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance.' Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) (Mere conclusions in appellants' brief that the claimed polymer had an unexpectedly increased impact strength "are not entitled to the weight of conclusions accompanying the evidence, either in the specification or in a declaration."); Ex parte C, 27 USPQ2d 1492 (Bd. Pat. App. & Inter. 1992) (Applicant alleged unexpected results with regard to the claimed soybean

plant, however there was no basis for judging the practical significance of data with regard to maturity date, flowering date, flower color, or height of the plant.).

Regarding newly added claims 95-142, since therapeutic efficacy is related to the amount (dosage) of active agent administered as well as timing of administration, it would have been obvious to one of ordinary skill in the art to further modify the methods of DiMartino such that SAHA is administered in an amount and for a period of time effective to optimize treatment of the leukemias.

Conclusion

Claims 1-10, 12-28, 30-36, 38-43, 45-50, 52-57, 59-63, 95-142 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-**

272-0572. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
April 17, 2006

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SUPERVISORY PATENT EXAMINER
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